

Amendments to the Drawings:

Replacement drawings that comply with the size requirements and that are clear and in permanent ink. The replacement contains the same material as the drawings filed on August 12, 2004 and on deposit. The attached replacement sheets of drawings include Figs. 1, 2, 3, 4A, 4B, 5, 6, 7A, 7B, 7C, 8, 9, 10, 11, 12, and 13.

Attachments following last page of this Amendment:

Replacement Sheet (14 pages)

### **REMARKS**

In reply to the Office Action mailed March 22, 2007, Applicants provided replacement drawings, amended the specification (including the title and abstract), and amended claims 1, 5, 7, 10-13, 25-27, 30, 31, and 34. Claims 1-31 and 34 are pending and under examination. Please consider the following remarks.

The drawings submitted August 17, 2004 were objected to as failing to be labeled as replacement drawings. Applicants submit herewith a set of drawings labeled as "replacement drawings" and request that the corresponding rejection be withdrawn.

The specification was objected to due to various informalities as provided on pages 3 and 4 of the Office Action. Applicants have amended the specification to address each of these informalities and request that the corresponding objections be withdrawn.

Claims 1-31 and 34 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. As provided in the Office Action, the Examiner asserts that the invention does not produce a useful, concrete and tangible result (See Office Action, page 6.). Applicants have amended independent claims 1, 30, 31, and 34 to provide in each instance a useful, concrete and/or tangible result. Specifically, Applicants have amended independent claims 1, 30, 31, and 34 to recite that "one or more of the output models be displayed." Support for these amendments can be found, for example, in Figure 1.

Claims 1-31 and 34 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants have amended the preamble of claims 1, 30, 31 and 34 to recite that the claimed methods, article and apparatus generate 3-D structural models of complex formation between a query ligand and a target molecule, which corresponds with the other steps as recited in the claims. Applicants have also amended "the comparison ligand" to recite "a" comparison ligand as identified in the previous step.

Independent claims 1, 30, 31, and 34 were also rejected based term "homologous," which is alleged to be "a relative term that renders the claims indefinite." (See Office Action, page 7.) Applicants have described examples of homologous macromolecules as can be used in the present invention in the paragraph beginning on page 11, line 5 of the specification. Exemplary characteristics for homologous macromolecules include as provided in the specification include sequence relatedness, three-dimensional relatedness, and a common fold or other secondary

structure. Applicants therefore submit that the term homologous, when read in the context of the application as a whole would be clear and therefore satisfy the requirements of 35 U.S.C. 112.

Dependent claims 5, 7, 9, 10, 11, 12, 13, 25, 27, 30, and 34 were rejected based on terms or phrases that are alleged to either lack antecedent basis or otherwise render the claim unclear. Applicants have amended claim 5 to recite that the output model also represent atoms in addition to those identified as sharing an identical substructure of the query ligand, removing the term “non-substructure atoms.” Applicants have amended claims 7, 11, and 12 to recite the substructure of the query ligand identified in b) comprises the information recited in the claim so as to provide antecedent basis. Applicants have amended claim 9 to provide “cyclic portions” of the recited framework, replacing the term “cyclic atoms” to provide antecedent basis for the term “cyclic portions” as used subsequently in the claim.

Applicants have amended claim 10 to recite that at least 5, 7, or 10 atoms in each ligand are identical to at least 5, 7, or 10 atoms in the comparison ligand(s), thus providing clarity as to the metes and bounds of the recited claim terms. Applicants have amended claim 13 to provide that it is the substructure, that is identified, as per step b), rather than the pharmacophore, giving antecedent basis for the term.

Applicants have amended claim 25 to clarify the intramolecular strain as recited in the claim, providing that the intramolecular strain energy is the strain energy undergone by the ligand to provide for binding between the substructure of the query ligand of b) and the target macromolecule. As shown above, Applicants also provided that the substructure is that of the query ligand recited in step b).

Applicants have amended claim 27 to recite that each of the ligands are assigned a preselected score, and to further recite that the samples are obtained based on an evaluation of the preselected score, clarifying both the relationship of each ligand to the preselected score and the relationship of the step of the obtaining of physical samples to the evaluating.

Applicants submit that claim 30 is sufficiently clear as presented. The step of executing cannot be taken by itself, but must be read within the claim as a whole. In reading the claim as a whole, Applicants submit that one skilled in the art would understand that instructions, as executed within an apparatus recited in the claims, would be executable by the apparatus. Removing the apparatus as a requirement for execution would not make sense when reading the

claim as a whole. In view of the foregoing, Applicants request that the corresponding rejection be withdrawn.

Applicants have amended claim 34 to replace the term “the compound” with the term “the ligand,” and to provide antecedent basis for the term “the test ligand.”

Applicants submit that the pending claims satisfy all statutory requirements and request that the application be placed in condition for allowance.

In response to the Notice of Non-Compliant Amendment mailed on January 8, 2009, Applicants submit the amendment described as follows. Applicants have added the amendments to the specification as included in the Amendment of September 24, 2007. Applicants have marked the title and Abstract to show changes made.

Applicants understand that these amendments are what the Examiner has requested. The amendments are intended to supersede any previous amendments made to the title, specification, and abstract. If these amendments do not address the issues raised in the Notice of Non-Compliant Amendment of January 8, 2009, Applicants request the Examiner telephone the undersigned so that any remaining formalities can be dealt with in the most expeditious manner.

Please apply any charges or credits to Deposit Account No. 50/2762, Ref. V2018-7001/10.

Respectfully submitted,  
Bemis et al., *Applicant*

By: /Catherine M. McCarty/  
Catherine M. McCarty, Reg. No. 54,301  
LOWRIE, LANDO & ANASTASI, LLP  
Riverfront Office Park  
One Main Street  
Cambridge, Massachusetts 02142  
Tel. (617) 395-7000

February 9, 2009  
925434